

PATENT DOCKET NO. P1219P3

WHAT IS CLAIMED IS:

- An isolated nucleic acid molecule which comprises DNA having at least about 80% sequence identity to (a) a DNA molecule encoding an FGF-19 polypeptide comprising the sequence of amino acid residues from about 1 or about 23 to about 216 of Figure 2 (SEQ ID NO:2), or (b) the complement of the DNA molecule of (a).
- The isolated nucleic acid molecule of Claim 1 comprising the sequence of nucleotide positions from about 464 or about 530 to about 1111 of Figure 1 (SEQ ID NO:1).
- The isolated nucleic acid molecule of Claim 1 comprising the nucleotide sequence of Figure 1 (SEQ ID NO: I).
- The isolated nucleic acid molecule of Claim 1 comprising a nucleotide sequence that encodes the sequence of amino acid residues from about 1 or about 23 to about 216 of Figure 2 (SEQ ID NO:2).
- 5. An isolated nucleic acid molecule comprising DNA which comprises at least about 80% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA deposited with the ATCC on November 21, 1997 under ATCC Deposit No. 209480 (DNA49435-1219), or (b) the complement of the DNA molecule of (a).
- The isolated nucleic acid molecule of Claim 5 comprising DNA encoding the same mature polypeptide encoded by the human protein cDNA deposited with the ATCC on November 21, 1997 under ATCC Deposit No. 209480 (DNA49435-1219).
- 7. An isolated nucleic acid molecule comprising DNA which comprises at least about 80% sequence identity to (a) the full-length polypeptide coding sequence of the human protein cDNA deposited with the ATCC on November 21, 1997 under ATCC Deposit No. 209480 (DNA49435-1219), or (b) the complement of the coding sequence of (a).
- The isolated nucleic acid molecule of Claim 7 comprising the full-length polypeptide coding sequence of the human protein cDNA deposited with the ATCC on November 21, 1997 under ATCC Deposit No. 209480 (DNA49435-1219).



PATENT DOCKET NO. P1219P3

- 9. An isolated nucleic acid molecule encoding an FGF-19 polypeptide comprising DNA that hybridizes to the complement of the nucleic acid sequence that encodes amino acids 1 or about 23 to about 216 of Figure 2 (SEQ ID NO:2).
- 10. The isolated nucleic acid molecule of Claim 9, wherein the nucleic acid that encodes amino acids 1 or about 23 to about 216 of Figure 2 (SEQ ID NO:2) comprises nucleotides 464 or about 530 to about 1111 of Figure 1 (SEQ ID NO:1).
- The isolated nucleic acid molecule of Claim 9, wherein the hybridization occurs under stringent hybridization and wash conditions.
- 12. An isolated nucleic acid molecule comprising at least about 22 nucleotides and which is produced by hybridizing a test DNA molecule under stringenthybridization conditions with (a) a DNA molecule which encodes an FGF-19 polypeptide comprising a sequence of amino acid residues from 1 or about 23 to about 216 of Figure 2 (SEQ ID NO:2), or (b) the complement of the DNA molecule of (a), and isolating the test DNA molecule.
- 13. The isolated nucleic acid molecule of Claim 12, which has at least about 80% sequence identity to (a) or (b).
 - A vector comprising the nucleic acid molecule of Claim 1.
- 15. The vector of Claim 14, wherein said nucleic acid molecule is operably linked to control sequences recognized by a host cell transformed with the vector.
- A nucleic acid molecule deposited with the ATCC under accession number 209480 (DNA49435-1219).
 - 17. A host cell comprising the vector of Claim 14.
 - 18. The host cell of Claim 17, wherein said cell is a CHO cell.
 - 19. The host cell of Claim 17, wherein said cell is an E. coli.

- 20. The host cell of Claim 17, wherein said cell is a yeast cell.
- 21. A process for producing an FGF-19 polypeptide comprising culturing the host cell of Claim 17 under conditions suitable for expression of said FGF-19 polypeptide and recovering said FGF-19 polypeptide from the cell culture.
- An isolated FGF-19 polypeptide comprising an amino acid sequence comprising at least about 80% sequence identity to the sequence of amino acid residues from about 1 or about 23 to about 216 of Figure 2 (SEQ ID NO:2).
- The isolated FGF-19 polypeptide of Claim 22 comprising amino acid residues from about 1 or about
 to about 216 of Figure 2 (SEQ ID NO:2).
- An isolated FGF-19 polypeptide having at least about 80% sequence identity to the polypeptide encoded by the cDNA insert of the vector deposited with the ATCC on November 21, 1997 as ATCC Deposit No. 209480 (DNA49435-1219).
- The isolated FGF-19 polypeptide of Claim 24 which is encoded by the cDNA insert of the vector deposited with the ATCC on November 21, 1997 as ATCC Deposit No. 209480 (DNA49435-1219).
- 26. An isolated FGF-19 polypeptide comprising the sequence of amino acid residues from about 1 or about 23 to about 216 of Figure 2 (SEQ ID NO:2), or a fragment thereof sufficient to provide a binding site for an anti-FGF-19 antibody.
- 27. An isolated polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding an FGF-19 polypeptide comprising the sequence of amino acid residues from 1 or about 23 to about 216 of Figure 2 (SEQ ID NO:2), or (b) the complement of the DNA molecule of (a), (ii) culturing a host cell comprising said test DNA molecule under conditions suitable for the expression of said polypeptide, and (iii) recovering said polypeptide from the cell culture.
- 28. The isolated polypeptide of Claim 27, wherein said test DNA has at least about 80% sequence identity to (a) or (b).

- A chimeric molecule comprising an FGF-19 polypeptide fused to a heterologous amino acid sequence.
- The chimeric molecule of Claim 29, wherein said heterologous amino acid sequence is an epitope tag sequence.
- The chimeric molecule of Claim 29, wherein said heterologous amino acid sequence is a Fc region
 of an immunoglobulin.
 - 32. An antibody which specifically binds to an FGF-19 polypeptide.
 - 33. The antibody of Claim 32, wherein said antibody is a monoclonal antibody.
 - 34. The antibody of Claim 32, wherein said antibody is a humanized antibody.
 - 35. The antibody of Claim 32, wherein said antibody is an antibody fragment.
 - 36. An agonist to an FGF-19 polypeptide.
 - An antagonist to an FGF-19 polypeptide.
- A composition of matter comprising (a) an FGF-19 polypeptide, (b) an agonist to an FGF-19 polypeptide, (c) an antagonist to an FGF-19 polypeptide, or (d) an anti-FGF-19 antibody in admixture with a pharmaceutically acceptable carrier.
 - 39. A method for screening for a bioactive agent capable of binding to FGF-19 comprising:
 - a) adding a candidate bioactive agent to a sample of FGF-19; and
- determining the binding of said candidate agent to said FGF-19, wherein binding indicates a bioactive agent capable of binding to FGF-19.
- 40. A method for screening for a bioactive agent capable of modulating the activity of FGF-19, said method comprising the steps of:

- a) adding a candidate bioactive agent to a sample of FGF-19; and
- (b) determining an alteration in the biological activity of FGF-19, wherein an alteration indicates a bioactive agent capable of modulating the activity of FGF-19.
- 41. A method according to Claim 40, wherein said biological activity is decreased uptake of glucose in adipocytes.
- A method according to Claim 40, wherein said biological activity is increased leptin release from adipocytes.
 - 43. A method according to Claim 40, wherein said biological activity is binding to FGF receptor 4.
- 44. A method of identifying a receptor for FGF-19, said method comprising combining FGF-19 with a composition comprising cell membrane material wherein said FGF-19 complexes with a receptor on said cell membrane material, and identifying said receptor as an FGF-19 receptor.
- 45. The method of Claim 44 wherein FGF-19 binds to said receptor, and said method further includes a step of crosslinking said FGF-19 and receptor.
 - 46. The method of Claim 44, wherein said composition is a cell.
 - 47. The method of Claim 44, wherein said composition is a cell membrane extract preparation.
- 48. A method of inducing leptin release from adipocyte cells, said method comprising administering

FGF-19 to said cells in an amount effective to induce leptin release.

- 49. The method of Claim 48, wherein said FGF-19 is administered as a protein.
- The method of Claim 48, wherein said FGF-19 is administered as a nucleic acid.
- 51. A method of inducing a decrease in glucose uptake in adipocyte cells, said method comprising administering FGF-19 to said cells in an amount effective to induce a decrease in glucose uptake.

- 52. The method of Claim 51, wherein said FGF-19 is administered as a protein.
- 53. The method of Claim 51, wherein said FGF-19 is administered as a nucleic acid.
- 54. A method of inducing an increase in insulin sensitivity in cells, said method comprising administering FGF-19 to said cells in an amount effective to induce an increase in insulin sensitivity.
 - 55. The method of Claim 54, wherein said FGF-19 is administered as a protein.
 - 56. The method of Claim 54, wherein said FGF-19 is administered as a nucleic acid.
- A method of treating an individual for obesity, said method comprising administering to said individual a composition comprising FGF-19 in an amount effective to treat said obesity.
- 58. The method of Claim 57, wherein said treatment of obesity further results in the treatment of a condition related to obesity.
 - 59. The method of Claim 58, wherein said condition is Type II diabetes.
 - 60. The method of Claim 57, wherein said FGF-19 is administered as a protein.
 - 61. The method of Claim 57, wherein said FGF-19 is administered as a nucleic acid.
- The method of Claim 57, wherein said composition further comprises a pharmaceutical acceptable carrier.
- 63. The method according to Claim 57, wherein said FGF-19 has at least about 85% amino acid sequence identity to the amino acid sequence shown in Figure 2 (SEQ ID NO:2).
- 64. A method of reducing total body mass in an individual, said method comprising administering to said individual an effective amount of FGF-19.

- 65. The method of Claim 64, wherein said FGF-19 is administered as a protein
- The method of Claim 64, wherein said FGF-19 is administered as a nucleic acid.
- The method of Claim 64, wherein said FGF-19 is administered with a pharmaceutical acceptable carrier.
- The method of Claim 64, wherein said reduction in total body mass includes a reduction in fat of said individual.
- 69. The method according to Claim 64, wherein said FGF-19 has at least about 85% amino acid sequence identity to the amino acid sequence shown in Figure 2 (SEO ID NO:2).
- 70. A method of reducing the level of at least one of triglycerides and free fatty acids in an individual, said method comprising administering to said individual an effective amount of FGF-19.
 - 71. The method of Claim 70, wherein said FGF-19 is administered as a protein.
 - 72. The method of Claim 70, wherein said FGF-19 is administered as a nucleic acid.
- 73. The method of Claim 70, wherein said FGF-19 is administered with a pharmaceutical acceptable carrier.
- 74. The method according to Claim 70, wherein said FGF-19 has at least about 85% annino acid sequence identity to the amino acid sequence shown in Figure 2 (SEQ ID NO:2).
- 75. A method of increasing the metabolic rate in an individual, said method comprising administering to said individual an effective amount of FGF-19.
 - 76. The method of Claim 75, wherein said FGF-19 is administered as a protein.
 - The method of Claim 75, wherein said FGF-19 is administered as a nucleic acid.

PATENT DOCKET NO P1219P3

- 78. The method of Claim 75, wherein said FGF-19 is administered with a pharmaceutical acceptable carrier.
- 79. The method according to Claim 75, wherein said FGF-19 has at least about 85% amino acid sequence identity to the amino acid sequence shown in Figure 2 (SEO ID NO:2).
 - 80. A rodent comprising a genome comprising a transgene encoding FGF-19.
- 81. A method of modulating the level of neuropeptide Y in a mammal, said method comprising administering to said mammal an effective amount of FGF-19, or an agonist or antagonist thereof.
 - 82. The method of Claim 81, wherein said FGF-19 is administered as a protein.
 - 83. The method of Claim 81, wherein said FGF-19 is administered as a nucleic acid.
- 84. The method of Claim 81, wherein said FGF-19 is administered with a pharmaceutical acceptable carrier.
- 85. The method according to Claim 81, wherein said FGF-19 has at least about 85% amino acid sequence identity to the amino acid sequence shown in Figure 2 (SEQ ID NO:2).
- 86. A method of modulating the level of agouti-related protein in a mammal, said method comprising administering to said mammal an effective amount of FGF-19, or an agonist or antagonist thereof.
 - 87. The method of Claim 86, wherein said FGF-19 is administered as a protein.
 - 88. The method of Claim 86, wherein said FGF-19 is administered as a nucleic acid.
- 89. The method of Claim 86, wherein said FGF-19 is administered with a pharmaceutical acceptable carrier.

PATENT DOCKET NO. P1219P3

- 90. The method according to Claim 86, wherein said FGF-19 has at least about 85% amino acid sequence identity to the amino acid sequence shown in Figure 2 (SEO ID NO:2).
- 91. A method of modulating the level of pro-opiomelanocortin in a mammal, said method comprising administering to said mammal an effective amount of FGF-19, or an agonist or antagonist thereof.
 - 92. The method of Claim 91, wherein said FGF-19 is administered as a protein.
 - 93. The method of Claim 91, wherein said FGF-19 is administered as a nucleic acid.
- 94. The method of Claim 91, wherein said FGF-19 is administered with a pharmaceutical acceptable carrier.
- 95. The method according to Claim 91, wherein said FGF-19 has at least about 85% amino acid sequence identity to the amino acid sequence shown in Figure 2 (SEO ID NO:2).